Chlorobenzenes - Comments of Environmental Defense

(Submitted via Internet 7/10/02)

Environmental Defense appreciates this opportunity to submit comments on the robust summary/test plan for Chlorobenzenes.

The SOCMA Chlorobenzene Producers Association prepared the test plan and robust summaries for a proposed category of 4 chlorobenzenes congeners. The proposed members are monochlorobenzene, 1,2-dichlorobenzene, 1,3-dichlorobenzene and 1,2,3-trichlorobenzene. In addition, data from two surrogate members are included to support the proposed category, namely 1,4-dichlorobenzene and 1,2,4-trichlorobenzene. This is a clearly written and informative test plan.

We do have some concerns over the proposed category particularly as it relates to the potential for distinct toxic properties of proposed members based on differential metabolism. It is well known that two adjacent unsubstituted carbon atoms are required for cytochrome P-450 hydroxylation so, for example, the hydroxylation sites for 1,2-dichlorobenzene will be different from those for 1,4-dichlorobenzene. This could cause significant differences in biological activity. Nevertheless, there is an abundance of available data for the proposed members with only a limited reliance on read-across interpolation of expected results. For this reason, we concur with the sponsor's assertion that no new mammalian toxicity studies are needed. However, we once again make the point that the scientific justification for category formation could be significantly enhanced if gene expression data were available to demonstrate a common pattern of molecular responses across a proposed category.

Two of the proposed members (monochlorobenzene and 1,2-dichlorobenzene) were studied by the NTP in long-term cancer bioassays as well as two-generation reproductive studies. The NTP concluded that these chemicals possessed no or weak carcinogenic or reproductive activity. A number of other well-conducted studies are available on the other 2 proposed members of this category. These studies indicate that the liver, kidney and thymus are target organs for monochlorobenzene and 1,2-dichlorobenzene, while the target organs for 1,3-dichlorobenzene include the pituitary and thyroid suggestive of endocrine activity not common for all proposed members. However, reproductive and developmental studies are available for 1,3-dichlorobenzene so even if it doesn't belong in this category, adequate data are available to fulfill the requirements of the HPV program.

Thank you for this opportunity to comment.

George Lucier, Ph.D.
Consulting Toxicologist, Environmental Defense

Karen Florini
Senior Attorney, Environmental Defense